leaves have also often been significantly more resistant to first-instar *M sexta* feeding than those from wild-type plants (Dowd PF and Lagrimini LM., unpublished). Intermediate-age leaves of transgenic tobacco and tomato typically show greater reductions in feeding relative to wild-type plants compared to very young, or very old leaves (Dowd PF and Lagrimini LM., unpublished).[5] Basal stems of *Nicotiana sylvestris* are significantly more resistant to feeding by *H zea* (as indicated by significantly higher insect mortality), while terminal stems are not.[1] Transgenic tobacco and tomato stems are also both significantly more resistant to feeding by *C lugubris* than wild-type stems.[1]

Sweetgum expressing tobacco anionic peroxidase showed significantly higher resistance to several species of insect compared to wild-type plants, which ranged from 1.6 × (for *O nubilalis*) to 31 × (for *H cunea*), but, as indicated previously, was more susceptible to feeding by *H zea*.[6] Although transgenic sweetgum significantly reduced growth rates of *L dispar* by 33%, and caused significantly less consumption relative to wild-type plants (21% reduction), this result was not related to any significant effect on the ability of the insects to digest the leaves.[6] However there was some indication that the transgenic leaves reduced the ability of the insects to convert digested food to biomass,[6] which could also be related to a toxic effect.

4 DISCUSSION

Although transgenic tissues expressing tobacco anionic peroxidase are generally more resistant to feeding by insects, insect age and species, and plant tissue type and age, can influence the degree of resistance noted (if any). The effect on insects feeding on transgenic tobacco and tomato relative to wild-type plants, which have relatively similar secondary metabolite profiles compared to sweetgum, was relatively consistent for the same insect species (Dowd PF and Lagrimini LM, unpublished).[1,5]

At present, most evidence suggests resistance is due to peroxidase-enhanced production of compounds toxic to the insects, as opposed to reducing nutritional quality or making tissues tougher (although these may be involved as well). When mortality occurs, it occurs at an interval shorter than that needed for caterpillars to starve to death when only water is provided.[1,5] If nutritional or structural effects were relatively more important than peroxidase production/detoxification of toxic metabolites for transgenic vs wild-type sweetgum, we would expect to see the same trend for *H zea* and *O nubilalis*.[6] The best evidence for the importance of a toxic effect is the detailed gravimetric nutritional studies performed with *L dispar* and sweetgum leaves.[6] In this instance, significant reductions of growth rates were noted, but these were not associated with significant effects on the insect's ability to digest or assimilate the leaves, suggesting that a toxic effect was most important.[6]

Although enhanced insect resistance by increasing peroxidase activity appears relatively consistent for the same insect species and tissues within the same plant genus[1,5] and family[1] (Dowd PF and Lagrimini LM, unpublished), enhanced resistance to insects through increased peroxidase activity can also potentially occur in distantly related dicotyledenous plants such as sweetgum.[6] Further study should yield answers to questions concerning appropriate peroxidase isozymes to express in suitable plant allelochemical environments for enhanced resistance to target insects.

ACKNOWLEDGEMENTS

We thank past and present students and technicians for technical assistance and MR McGuire for comments on prior drafts of this manuscript.

Names are necessary to report factually on available data; however, the USDA neither guarantees nor warrants the standards of the products, and the use of names by USDA implies no approval of the products to the exclusion of others that may also be suitable.

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Natural pesticides and the evolution of food plants

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Abstract: Cyanogenesis, a naturally occurring pesticide, played an essential role in the origin of plant agriculture. When our ancestors were domesticating plants, they chose a disproportionate number of cyanogenic species.

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Keywords: Food plants; cyanogenesis; natural products

Co-evolution between insects and flowering plants has been one of the major ongoing events in the development of life on earth.[1] The interactions involved are not exclusively those between flower and pollinator. Elaborate interactions have developed between plants, herbivorous insects and insect parasites, with fungi, mammals, molluscs and other herbivores complicating the situation still further. The secondary compounds produced by plants in profuse diversity are part of this extensive network of interactions,[2] although it is rarely easy to demonstrate either the origin or the present logistics of these interactions.[3] Genetical differences between plants of the same species have helped to clarify the situation in a small number of special cases, proving that some secondary compounds are part of the defence by plants against herbivores.[4] I have explained the difficulties involved with research of this kind elsewhere,[3] but the system I have been studying is amenable to analysis by methods of ecological genetics and chemical ecology.[4]

Within the past 25 years there has been an explosion of interest in ethnobotany, ethnopharmacology and now ethnopesticides,[5] as well as with the elaboration of the chemical aspects of old disciplines like plant pathology and emerging ones such as chemical ecology. The broad-based interdisciplinary nature of these studies has created problems of compatibility between researchers approaching similar investigations from fundamentally different basic disciplines. Constructive cooperation is emerging, but the wheel has been reinvented numerous times – to the chagrin of plant pathologists and ecologists.

In the context of pesticide science, chemical ecology concentrates on the natural chemical reactions between species sharing the same habitat, not on the challenging of pests with natural or synthetic compounds they would not normally meet in nature. Using humans as an example, chemical interactions between plants and humans have been, and remain, fundamental to the choice of our food plants, whether they be staple, exotic or casual foods. Chemical ecology is beginning to explain these interactions in other species and so indirectly help to explain human food choice during the past 15 000 years.

Today, much of the relevant research is based on individual plants of nutritional, pharmacological or pesticide importance. A recent book on natural pesticides demonstrates this well. Studies of the evolution of crop plants is, again, largely based on individual plants,[6,7] not on the concept of a balanced diet. The questions asked are: what plants do we eat and where and how have the plants we eat today evolved (been selected)?[7–9] Very few people have attempted to answer the question: why do humans[8] and other primates[10] have such restricted food ranges?

Animals eat very few of the other organisms with which they come into contact and so it is very reasonable to ask why they eat particular plants and animals and not others. Ethological studies reveal that most animals are remarkably good at choosing a balanced diet (eg Reference 10) and certainly the common human food plants contain the five major components of a balanced diet – carbohydrates, proteins, lipids, nucleic acids and vitamins. It is common knowledge that problems can arise when humans try foods outside the normal range, eat too much of the same food, or when natural pesticides, derived from plants other than those on our usual menu, are used to defend our normal food against pests. Medicinal plants are also in this category.

The obvious question now is: why do we have such a restricted range of food plants? A supplementary question is: what has been the role of chemistry in our choice of these food plants? These are the same questions for which Milton has some answers with other primates.[10] The literature of phytochemistry and chemical ecology contains an enormous amount of information about the role of secondary compounds in plant defence against herbivores, pathogens and pests[2] although, as indicated above, it is often difficult to provide absolute proof in many cases. Beyond reasonable doubt, however, the hydrogen cyanide and aldehydes/ketones produced by a cyanogenic plant when it is damaged are part of the defence by these plants against casual herbivores.[4] Hydrogen cyanide is highly toxic to humans. Thus it is surprising to find that 16 of the 24 most important human food plants are cyanogenic (Table 1, updated from Reference 11). The best independent evidence suggests that the list should contain no more than three.[11,12] I have explained elsewhere that cyanogenesis is a remarkably effective defence against casual herbivores.[4] Furthermore, there is good evidence that many of our food plants are indeed defended by cyanogenesis against pests,[11] although cyanogenesis is noticeably absent

Table 1. Cyanogenesis and world production of major food crops in 1996

Crop[a]	*Production (10^6 tonnes)*	*Crop*[a]	*Production (10^6 tonnes)*
Maize	588.2	**Wheat**	586.1
Paddy rice	569.9	Potatoes ?	306.0
Cassava	165.6	**Barley**	157.0
Sweet potato	138.4	Soya beans ?	129.1
Raw sugar	126.8	*Tomatoes*	88.7
Sorghum	69.1	Oranges ?	58.7
Bananas ?	57.7	**Apples**	55.5
'Pulses'	54.1	*Cabbage*	49.5
Watermelon	44.7	*Coconuts*	44.6
Onions, dry ?	37.5	**Yams**	32.1
Oats	31.1	**Rapeseed**	30.6
Peanuts	30.2	**'Millets'**	28.8

[a] **Bold** – cyanogenic; **?** not known to be cyanogenic, but there are cyanogenic species in the same genus; *italics* – cyanogenesis not known in genus.

Source: Food and Agriculture Organization, Quarterly Bulletin of Statistics 10, 3/4, 1997.

from those discussed by Prakash and Rao.[5] The system is thought to be too complex, involving at least two components – substrate and enzyme – for us to use it commercially, and single compounds were the basis of the book.[5] The present state of biotechnology may be too primitive to effect the transfer of the genetic systems involved into other plants, in spite of recent wishful thinking.[13] Furthermore, because so many of our food plants are already cyanogenic, it may not be sensible to attempt to transfer cyanogenesis into those few important ones that are not.

The data from a large number of sources show that cyanogenesis appears to have played an essential part in the choice of the major food plants by humans at the time of transition from hunter-gatherer to cultivator and husbandman.[11] The evidence is based on the following observations (see Reference 11 for details): (1) Our food plants have to be ones we can eat in quantity. Most other potential food plants contain compounds that we cannot detoxify or metabolize in quantity. We have found other uses for some of these compounds. In small doses, many are medicinal drugs, although in larger doses they are metabolically dangerous. (2) Our food plants have to be easy to grow with minimal care and attention, and 'good' to eat. (3) The cyanogenesis of the leaves deters many would-be pests. A plant with few pests would be an attractive candidate for domestication by our ancestors. These plants are not difficult to grow as crops and could well have been higher-yielding than other candidates not similarly protected. (4) Given sufficient protein we can detoxify the hydrogen cyanide released by raw cyanogenic plants, so long as they are only part of a meal. (5) By processing the food before eating we can remove most of the hydrogen cyanide and the cyanogenic compounds and so eat much more. Very few other organisms pre-process food, not even our primate relatives.[10] (6) Our domesticated animals can also detoxify hydrogen cyanide, again given sufficient protein in the diet. (7) It is the leaves of our cereal crops that are cyanogenic, not the grains. We eat the grain, our animals may eat the rest. (8) Cyanogenic glycosides and the β-glycosidases are economical compounds for plants to produce; they are turned over in the plant and are used only when the plant is damaged. (9) Although cyanogenic glycosides are arguably the most widespread of all chemical defences in vascular plants and, when degraded, are remarkably effective herbivore deterrents (pesticides), we have included a disproportionally large number of cyanogenic plants among our staple foods.

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Bis-pyrimidylpyrazolinones – a new class of acetohydroxy-acid synthase (AHAS) inhibitor

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Abstract: Hydroxypyrazolinones which bear two pyrimidine rings (on N-1 and C-4) were found to be potent inhibitors of acetohydroxy-acid synthase which displayed good herbicidal activity *in vivo*. Structure–activity relationship studies suggested the presence of a second binding niche on the enzyme for a 4,6-dimethoxypyrimidine ring.

Keywords: acetohydroxy-acid synthase; dimethoxypyrimidine; herbicide; pyrazolinones; structure–activity relationship

1 INTRODUCTION

In random screens, 1-(3,5-dichlorophenyl)-4-isobutylpyrazolidine-3,5-dione was identified as a moderate herbicide lead which induced symptoms on the plants consistent with the inhibition of acetohydroxy-acid synthase (AHAS). Analog synthesis first concentrated on pyrimidine replacements of the phenyl ring. As an unexpected reaction product, a pyrazolinone was obtained which bore pyrimidine rings on N-1 and C-4. Surprisingly, this new compound was significantly more active than previous analogs. A standard enzyme assay confirmed AHAS inhibition as the primary mode of action.

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(*Received 1 July 1998; accepted 1 February 1999*)